



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PURIFICATION OF:

Roberts et al.

SERIAL NO.: 08/304,147

) GROUP ART UNIT

FILING DATE: 9/12/94

) EXAMINER

RE: Method and Compositions To  
Assess Oxidative Stress  
In Vivo

The Honorable Commissioner of  
Patent and Trademark  
Washington, D.C. 20231

Sir:

**132 DECLARATION**

I, Lawrence J. Marnett, declare:

1. I received my B.S. degree from Rockhurst College in 1969, and my Ph.D from Duke University in 1973. I am currently the Mary Geddes Stahlman Professor of Cancer Research, Professor of Biochemistry, and Professor of Chemistry at Vanderbilt University. I am Director of the A.B. Hancock, Jr. Memorial Laboratory for Cancer Research and Research Director of The Vanderbilt Cancer Center. I have been a member of the editorial boards of nine scientific journals including the Free Radical Biology and Medicine (1985-1994). I am currently Editor-in-Chief of Chemical Research in Toxicology. I have been actively involved in research in the areas of prostaglandins and free radicals for over 20 years. My curriculum vitae is attached hereto as Exhibit A.

2. I have reviewed the above-captioned application and Morrow et al., "Noncyclooxygenase Oxidative Formation of a Series of Novel Prostaglandins: Analytical Ramifications for Measurement of Eicosanoids," Anal. Biochem. 184:1-10 (1990).

3. The above application discloses that a series of prostaglandin F<sub>2</sub>-like compounds, now referred to as isoprostanes, are produced in vivo by a free radical catalyzed process. The application also discloses that these prostaglandin F<sub>2</sub>-like compounds can be detected in normal human biological fluids and that their formation increases dramatically in settings of oxidant stress in vivo. The application claims methods for assessing oxidative stress in vivo by quantification of these prostaglandin F<sub>2</sub>-like compounds.

4. The discovery by the Applicants that prostaglandin F<sub>2</sub>-like compounds were produced *in vivo* was surprising because it demonstrated that compounds related to prostaglandins could be formed chemically instead of enzymatically.

5. Prior to the Applicants' discovery there was no convincing evidence that free radical-catalyzed peroxidation of lipids actually occurred *in vivo*. This was hotly debated and the balance of opinion was that if peroxidation did occur *in vivo* it could only be demonstrated in animal models treated with extremely toxic agents designed to trigger oxidative stress. However, Applicants demonstrated that this process occurs in normal human beings not treated with unusual or toxic agents. Furthermore, Applicants showed that lipid peroxidation increases in human beings in some clinical and lifestyle conditions (e.g.

smoking). Additionally, Applicants demonstrated the ability to discriminate renal production of isoprostanes from systemic production of isoprostanes and to detect the production of isoprostanes in individual tissues. Roberts et al. provided the first convincing evidence that peroxidation occurred *in vivo*. Their finding were stunning to the scientific community, even to experts in the field of oxidative stress.

I hereby declare that all statements made herein are believed to be true; and further, these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of this application or any patent issuing thereon.

Dated 11/23/94

Lawrence J. Marnett  
Lawrence J. Marnett



## CURRICULUM VITAE

Name

Lawrence J. Marnett

Social Security

511-52-1113

Born

Kansas City, Kansas - November 22, 1947

Citizenship

USA

Marital Status:

Married, Two children

Campus Address

Department of Biochemistry  
Vanderbilt University School of Medicine  
Nashville, TN 37232  
(615) 343-7329

Education

B.S., Rockhurst College, *cum laude*, 1969

Ph.D., Duke University, 1973

Dissertation: "*The Thermal and Photochemical Decomposition of Unsymmetric Azo Compounds*" Professor Ned A. Porter, Advisor

### Professional Positions

*Research Associate*, Karolinska Institutet, in collaboration with Professor Bengt Samuelsson, 1973-1974

*Research Associate*, Wayne State University, in collaboration with Professor A. Paul Schaap, 1974-1975

*Assistant Professor Chemistry*, Wayne State University, 1975-1980; *Associate Professor of Chemistry*, Wayne State University, 1980-1983; *Professor of Chemistry*, Wayne State University, 1983-1989

*Mary Geddes Stahlman Professor of Cancer Research, Professor of Biochemistry, Professor of Chemistry*, Vanderbilt University School of Medicine, 1989-

*Director*, A.B. Hancock, Jr. Memorial Laboratory for Cancer Research, Vanderbilt University School of Medicine, 1989-

*Associate Director for Basic Science*, The Vanderbilt Cancer Center, 1993-

### Awards and Honors

Probus Club Award for Academic Achievement (1980)

Wayne State University President's Award for Excellence in Teaching (1980)

American Cancer Society Faculty Research Award (1982)

Sigma Xi Research Award (1986)

Wayne State University Distinguished Graduate Faculty Award (1988)

Michigan Association of Governing Boards Distinguished Faculty Award (1988)

National Cancer Institute Outstanding Investigator Grant (1988-1995)

## Scientific Societies

American Chemical Society  
American Society of Biochemistry and Molecular Biology  
American Association for the Advancement of Science  
International Society for the Study of Xenobiotics  
American Association for Cancer Research  
Society of Toxicology  
The Oxygen Society - Fellow

## Honorary Societies

Alpha Sigma Nu  
Phi Lambda Upsilon  
Sigma Xi

## Professional Activities

*Member*, Species Comparison in Carcinogenesis Study Section (ad hoc), National Institutes of Health, 1981.

*Visiting Associate Professor of Biochemistry*, University of Texas Health Science Center at Dallas, 1981.

*Member*, Chemical Pathology Study Section, National Institutes of Health, 1982-1985.

*Organizer*, Symposium on Arachidonic Acid Metabolism, American Chemical Society National Meeting, Chicago, Illinois, 1985.

*Visiting Scholar*, University of Toledo, Department of Chemistry, 1986.

*Coorganizer*, Symposium on Peroxidase Mechanisms in Chemical Carcinogenesis, Federation of American Societies for Experimental Biology. Annual Meeting, St. Louis, Missouri, 1986.

*Organizing Committee*, International Conference on Anticarcinogenesis and Radioprotection, Rockville, Maryland, 1987.

*Organizing Committee*, Gordon Conference on Oxygen Radicals in Biology and Medicine, Santa Barbara, California, 1987.

*Member*, Medical Biochemistry Study Section (ad hoc), National Institutes of Health, 1988.

*Vice-Chairman*, Gordon Conference on Oxygen Radicals in Biology and Medicine, Santa Barbara, California, 1989.

*Organizing Committee*, Eicosanoids and Bioactive Lipids in Cancer & Radiation Injury - 1st International Conference, Detroit, Michigan, 1989

*Chairman*, Gordon Conference on Oxygen Radicals in Biology and Medicine, Santa Barbara, California, 1990.

*International Advisory Committee*, Seventh International Conference on Prostaglandins and Related Compounds, Florence, Italy, 1990

*International Scientific Advisory Committee*, International Symposium on Biological Oxidation Systems, Bangalore, India, 1989

*Organizing Committee*, Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Radiation Injury - 2nd International Conference, Berlin, West Germany, 1991

*Program Advisory Committee*, Prostaglandins, Leukotrienes and Lipoxins, Washington, D.C., 1991

*International Advisory Committee*, Montreal Conference on Prostaglandins and Related Compounds, Montreal, Canada, 1992

*Organizer*, Symposium on Peroxidases and Peroxyl Radicals in Toxicity, Society of Toxicology Meeting, Seattle, Washington, 1992

*Program Committee*, Thirteenth Enzyme Mechanism Meeting, Key Largo, Florida, 1993  
*Organizing Committee*, Third International Meeting on Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Radiation Injury - Washington, D.C. 1993  
*International Advisory Committee*, 9th International Conference on Prostaglandins and Related Compounds, Florence, Italy, 1994  
*Coorganizer*, American Cancer Society Workshop on NSAID's and Colon Cancer Prevention, Atlanta, Georgia, 1994  
*Coorganizer*, Symposium on Arachidonic Acid Metabolism, Chemical Congress of Pacific Basin Societies, Honolulu, Hawaii, 1995

### **Editorial Activities**

Member, Editorial Board, *The Journal of Biological Chemistry*, 1983-1987.  
Member, Editorial Board, *Archives of Biochemistry and Biophysics*, 1984-1993  
Member, Editorial Board, *Cancer Research*, 1985-1986.  
Member, Editorial Board, *Free Radical Biology and Medicine*, 1985 -1994  
Member, Editorial Board, *Carcinogenesis*, 1986-1988  
Member, Editorial Board, *Advances in Pharmacology*, 1987-  
Series Co-Editor, *Prostaglandins, Leukotrienes, and Cancer*, Martinus-Nijhoff Publisher, 1984-  
Editor-in Chief, *Chemical Research in Toxicology*, 1987-  
Member, Editorial Board, *Redox Reports*, 1994-1996

### **Graduate Degrees Directed**

#### *M.S.*

Bienkowski, Michael, M.S., 1980  
*"Oxygen-18 Investigation of the Arachidonic Acid Dependent-Coxygenation of Xenobiotics"*

Prust, Robert M., M.S., 1981  
*"Test for the Intermediacy of 11-Hydroperoxy-Arachidonic Acid in Prostaglandin Biosynthesis"*

Wilhelm, Jeffrey, M.S., 1986  
*"The Cooxidation of Nafazatrom by Prostaglandin H Synthase"*

George, Alister, M.S., 1987  
*"A Method for In Situ Generation of Prostaglandin H<sub>2</sub>"*

Carolin, Kathryn, M.S., 1989  
*"Synthesis of Site-Specific 1,N<sub>2</sub>Ethenodeoxyguanosine in a Small Oligonucleotide"*

Laudicina, D.C., 1989  
*"Synergistic Stimulation of Lipid Peroxidation by Organic Hydroperoxides and Ascorbate"*

#### *M.A.*

DeSantis, Nancy, M.A., 1988

#### *Ph.D.*

Page, William R., Ph.D., 1981

"The Peroxidase Activity of Prostaglandin Endoperoxide Synthetase"

Reed, Gregory A., Ph.D., 1981

"Metabolism and Activation of Benzo[a]pyrene and Benzo-Ring Derivatives During Prostaglandin Biosynthesis"

Dix, Thomas, Ph.D., 1983

"The Mechanism of the Fatty Acid Hydroperoxide Dependent-Epoxidation of 7,8-Dihydroxy-7,8-Dihydrobenzo[a]pyrene"

Basu, Ashis, Ph.D., 1984

"Studies on the Mutagenicity of Malondialdehyde and Related Compounds"

Weller, Paul E., Ph. D., 1985

"Chemical and Enzymatic Transformations of 5-Phenyl-4-Pentenyl-1-Hydroperoxide"

Battista, John R., Ph.D., 1986

"The Role of Hydroperoxide-Dependent Oxidations in the Metabolic Activation of Chemical Carcinogens"

Bull, Arthur W., Ph.D., 1986

"Lipid Peroxidation and Intestinal Carcinogenesis: Structure-Activity Relationships and Analytical Methods"

Samokyszyn, Victor, M., Ph.D., 1987

"Oxidation of 13-Cis-Retinoic Acid by Iron-Oxo Intermediates of Prostaglandin H Synthase and Unsaturated Fatty Acid-Derived Peroxyl Radicals"

Labeque, Regine, Ph.D., 1988

"Reaction of Allylic Hydroperoxides With Metals and Metalloproteins"

Markey, Christine M., Ph.D., 1988

"Interaction of the Peroxidase and Cyclooxygenase Activities of Prostaglandin H Synthase: Characterization of the Peroxidase"

O'Hara, Shawn M., Ph. D., 1988

"Studies on the Reaction of  $\beta$ -Alkoxy-Acroleins With Guanine Nucleosides and Frameshift Mutagenesis in *Salmonella typhimurium hisD3052"*

Plé, Patrick, Ph.D., 1988

"Structure-Activity Studies of Alkyl Aryl Sulfides and Related Compounds as Reducing Substrates for the Peroxidase Activity of Prostaglandin H Synthase"

Chen, Ying Nan Pan, 1988

*Studies on the Structure and Function of Prostaglandin H Synthase*

Stone, Koni K., 1990

*Studies of the Reaction of Malondialdehyde with Nucleosides*

Reddy, Ashok, 1990

*Separation of (+)-Syn and (-)-Anti-Benzo[a]pyrene Dihydrodolepoxyde-DNA Adducts in [32P]-Postlabeling Analysis: Application to the Study of Pathways of Benzo[a]pyrene Metabolism in Mouse Skin In Vivo*

Odenwaller, Rebecca, 1991

*Studies on the Role of the Peroxidase of Prostaglandin H Synthase in Its Cyclooxygenase Reaction"*

Benamira, Mounir, 1992

*Mutagenesis by Malondialdehyde. Random and Site-Specific Approaches to the Role of Individual DNA Adducts*

Wells, Isabelle, 1992

*Chemical Modification of Prostaglandin H Synthase by N-Acetylimidazole and Reactive Indomethacin Derivatives*

Chapeau, Marie-Christine, 1992

*Strategies for Construction of Carcinogen Adducts of Deoxynucleosides*

### **Administrative Activities**

#### *Wayne State University*

Chairman, Education Committee, American Chemical Society, Detroit Section, 1976-1977.

Alternate Councilor, American Chemical Society, 1978-1980.

Graduate Recruiting Officer, Department of Chemistry, 1980-1982.

Personnel Committee, Department of Chemistry, 1981-present.

Member, Chairman Search Committee, Biochemistry Department, Wayne State University School of Medicine, 1985.

External Program Review, Eppley Institute for Cancer Research, University of Nebraska, 1985.

Comprehensive Cancer Center of Metropolitan Detroit, Developmental Grants Review Board, 1984-present.

Member, Molecular Biology Center Advisory Committee, Wayne State University, 1985-1988.

Member, Dean Search Committee, College of Pharmacy and Allied Health, Wayne State University, 1987

University Grant Review Committee, Science Subcommittee, 1987

External Program Review, Toxicology Program, University of California San Francisco, 1987

Wayne State University Biomedical Research Committee, 1988

Nominating Committee, Society of Toxicology, Molecular Biology Specialty Section, 1988

*Vanderbilt University*

Cancer Center Advisory Committee, 1989-  
Ernest Goodpasture Chair in Experimental Pathology Search Committee, 1990-  
American Chemical Society, Nashville Section, Program Committee, 1990  
Medical Oncology Division Chairman , Department of Medicine, Search Committee, 1990-1992  
Pediatric Pulmonary Specialized Center of Research, Scientific Advisory Committee, 1990-  
American Association of Cancer Research, "Minuteman" Scientific and Public Education  
Committee, 1990-  
American Cancer Society Institutional Research Grant Committee, 1990-; Chairman, 1994-  
School of Medicine, Institutional Self-Study, Research Committee, 1991  
Biomedical Science Seminar Committee, 1991  
Biochemistry Department Graduate Education Committee, 1991-  
Chemistry Department Divisional Organization Committee, 1990  
American Association for Cancer Research, G.H.A. Clowes Award Committee, 1991  
American Association for Cancer Research, Publications Committee, 1991-1994  
American Association for Cancer Research, Publications Committee, Chairman, 1994-1997  
Biochemistry Department Committee on Curriculum Design, 1992  
Clinical Pharmacology Center Executive Committee, 1992-  
External Advisory Committee, Program Project in Sickle Cell Biology, University of Chicago,  
1992-  
Toxicology External Advisory Committee, University of Arizona, 1992-  
Vanderbilt Cancer Center Advisory Board, 1993-  
National Institute of Environmental Health Sciences Review Committee, 1993  
Vanderbilt Cancer Center Research Programs Committee, Co-Chairman, 1994-  
Vanderbilt Cancer Center Shared Resources Committee, Chairman, 1994-

**Teaching**

*Wayne State University*

Chem 100 Chemistry for Non-Science Majors  
Chem 101 General Chemistry for Occupational Therapists  
Chem 103 General Chemistry for Pre-Nursing Students  
Chem 105 General Chemistry  
Chem 560 Introductory Biochemistry  
Chem 660 Advanced Biochemistry  
Chem 878 Enzyme Mechanism  
Chem 879 Chemical Carcinogenesis

*Vanderbilt University*

Bio 321 Basic and Advanced Biochemistry  
Bio 336 Biochemical Toxicology and Carcinogenesis  
Bio 337 Student Seminar  
Bio 337 Molecular Aspects of Cancer Research  
Bio 301 Molecular Structure and Function

### Ph.D. Committees

#### *Vanderbilt University*

Christopher Smith  
Anita Corbett  
Megan Robinson  
Stephanie Dew  
Michael McCarthy  
Christopher Smith  
Kevin Raney  
Liang Zhou  
Seong Jin Kim  
Karen Richards  
Kristin Johnson  
Laura Neiderhofer  
Sandra Miller-Davis  
Bin-Bin Fang  
Jason Weisenseel  
S. Krisnaswamy  
David Johnston  
Gary Latham  
Cheryl Lanzo  
Stephen Fink  
Merilyn Blair  
Kathy Wheeler  
Sin Han  
Eleanor McCarthy  
David Ferguson

### Consulting Activities

Searle and Co., 1981  
Warner-Lambert/Parke-Davis, 1982  
Oxford Biomedical Research, 1984-present  
Searle and Co., 1985  
Health Effects Institute, 1985-1987  
Proctor and Gamble, 1987  
Searle and Co., 1988  
Proteins International, 1987-present  
Monsanto, 1993-

### Previous Research Support

Wayne State University, "Faculty Research Award" Direct Costs: 6/1/76-8/31/76, \$6,000.

American Chemical Society - Petroleum Research Fund, "The Oxygenation of Polycyclic Aromatic Hydrocarbons by Prostaglandin Synthetase" Direct Costs: 6/1/76-8/31/79, \$9,000.

American Cancer Society, BC-244 "The Role of Prostaglandin Synthetase in the Metabolic Activation of Chemical Carcinogens" 1/1/77-12/31/88, \$625,836.

National Institutes of Health, R01-GM 23642 "Studies on Prostaglandin Synthase" Direct Costs: 1/1/77-6/30/90, \$750,000.

National Institutes of Health, R01-CA 22206 "Studies on Malondialdehyde" Direct Costs: 8/1/77-4/30/88, \$595,415

Merck and Co., "Studies on Prostaglandin Synthetase" Direct Costs, 9/1/77-8/31/78, \$10,000.

Searle and Co. "Malondialdehyde Levels in Human Cervical Mucous" Direct Costs: 9/1/81-8/31/83, \$71,000

Miles Institute for Preclinical Pharmacology, "Metabolism of Nafazatrom" Direct Costs: 7/1/82-6/30/83, \$30,000.

National Institutes of Health, R01-CA 32506 "Cancer Chemoprevention and Arachidonate Metabolism" Direct Costs: 8/1/82-6/30/85, \$106,278.

American Cancer Society, FRA-243 "Faculty Research Award" Direct Costs: 9/1/82-9/1/87, \$150,000

National Institutes of Health, R01-CA 43209 "Peroxyl Radicals, Hydroperoxides, and Carcinogenesis" Direct Costs: 8/1/86-7/31/88, \$153,998.

Harper Hospital, "Mechanisms of Metastasis" Coinvestigator with K. Honn, C. Johnson, and B. Sloane, Direct Costs: 9/1/85-12/31/87, \$575,000.

Thomae Pharmaceuticals, "Studies on Metastasis" Direct Costs: 4/1/86-9/30/87, \$60,000.

Wayne State University, IPPRI Program, "Construction of Protein Conjugates of Difunctional Carbonyl Compound Adducts to Nucleosides for Production of Immunochemical Reagents for Molecular Dosimetry" Direct Costs: 4/1/87-3/31/88, \$22,000.

Thomae Pharmaceuticals, "Studies on Metastasis" Direct Costs: 4/1/87-9/30/88, \$55,000.

Wayne State University, Center for Chemical Toxicology, "Investigation of Hydroperoxide Formation and Metabolism During Mouse Skin Tumor Promotion" Direct Costs: 5/1/88-4/30/89, \$29,850.

Ono Pharmaceutical, "Studies on 12-Lipoxygenase" Direct Costs: 1/1/88-12/31/92, \$434,000.

#### Current Research Support:

National Institutes of Health, R35-CA 47479-05 "Outstanding Investigator Grant - Polyunsaturated Fatty Acid Metabolism and Carcinogenesis" Direct Costs: 6/15/94-3/31/95, \$493,773; 4/1/95-3/31/01, \$3,899,965

**Invited Symposium Lectures:**

*American Society of Photobiology Workshop on Chemiluminescence and Lipid Peroxidation*, Colorado Springs, Colorado (February 22, 1980).

*10th Linderstrom-Lang Conference*, Skokloster, Sweden (June 20-23, 1980).

*Gordon Conference on Drug Metabolism*, Plymouth, New Hampshire (July 21-25, 1980).

*Gordon Conference on Oxygen Radicals in Biology & Medicine* Ventura, California (January 12-16, 1981).

*Winter Prostaglandin Meeting*, Clearwater, Florida (March 1-5, 1981).

*International Symposium on Metabolism and Pharmacokinetics of Environmental Chemicals in Man*, Sarasota, Florida (June 8-12, 1981).

*National Cancer Institute Workshop on Chemoprevention of Carcinogenesis*, Bethesda, Maryland (June 25-26, 1981).

*International Conference on Prostaglandins and Cancer*, 1981, Washington, D. C. (August 31-September 3, 1981).

*Symposium on Nafazatrom*, Port Chester, New York (October 1-2, 1981).

*V International Conference on Prostaglandins*, Florence, Italy (May 18-22, 1982).

*Conference on Enzyme Chemistry*, Northwestern University Medical School, Evanston, Illinois (June 17, 1983).

*Gordon Research Conference on Drug Metabolism*, New Hampshire (July 29, 1983).

*Workshop on Eicosanoids*, University of Michigan, Ann Arbor, Michigan (October 20, 1983).

*Symposium on Comparison of Radiation and Chemically-Induced Cancer*, National Cancer Institute, Gaithersburg, Maryland (December 6-8, 1983).

*Chemoprevention Workshop*, National Cancer Institute, Bethesda, Maryland (May 4, 1984).

*Mechanisms of Metastasis*, Detroit, Michigan (June 2, 1984).

*Ninth European Workshop on Drug Metabolism*, Pont a Mousson, France (June 13, 1984).

*Symposium on Polycyclic Hydrocarbons and Cancer*, American Chemical Society, Philadelphia, Pennsylvania (August 29, 1984).

*Workshop on the Role of Cyclic Nucleic Acid Adducts in Mutagenesis and Carcinogenesis*, Lyon, France (September 18, 1984).

*Kyoto Conference on Prostaglandins*, Kyoto, Japan (November 27, 1984).

*Prostaglandin Biochemistry Workshop*, Otsuka Research Institute, Tokushima, Japan (November 29, 1984).

*Workshop on Oxygen Radicals and Cancer*, Berkeley, California (February 8-9, 1985).

*Gordon Conference on Oxy-Radicals in Biology and Medicine*, Santa Barbara, California (February 11-15, 1985).

*American Association for Cancer Research Symposium on Non-Cytochrome P-450-Mediated Carcinogen Metabolism and Activation*, Houston, Texas (May 25, 1985).

*Gordon Conference on Free Radicals*, Plymouth, New Hampshire, (June 10-14, 1985).

*Symposium on Arachidonic Acid Metabolism*, American Chemical Society, Chicago, Illinois (September 11, 1985).

*Symposium on Health Effects of Automotive Emissions*, Dearborn, Michigan (November 1, 1985).

*Symposium on Radical-Induced Damage to DNA*, Michigan State University, East Lansing, Michigan (November 9, 1985).

*US-Japan Cooperative Meeting on Oxygen Radicals and Cancer*, Makaha, Hawaii (March 27-28, 1986).

*FASEB Symposium on Peroxidase Mechanisms in Chemical Carcinogenesis*, St. Louis, Missouri (April 15, 1986).

*VI International Conference on Prostaglandins*, Florence, Italy (June 3-6, 1986).

*FASEB Summer Research Conference on Lung Pharmacology and Pathophysiology*, Saxton's River, Vermont (July 27-August 1, 1986).

*National Cancer Institute Workshop on Free Radicals and Cancer*, Santa Barbara, California (February 8, 1987).

*Gordon Conference on Oxy-Radicals in Biology and Medicine*, Santa Barbara, California (February 9-13, 1987).

*American Cancer Society Workshop on Mechanisms of Tumor Promotion*, Key Biscayne, Florida (February 23-25, 1987).

*Second International Conference on Anticarcinogenesis and Radioprotection*, Gaithersburg, Maryland (February 9-12, 1987).

*Winter Prostaglandin Meeting*, Orlando, Florida (March 12-14, 1987)

*Gordon Conference on Cancer*, New London, New Hampshire (August 17-21, 1987)

*UCLA Symposium on Oxygen Radicals in Molecular Biology and Pathology*, Park City, Utah (January 25-29, 1988)

*Society for Free Radical Research International Conference on Medical, Biochemical and Chemical Aspects of Free Radicals*, Kyoto, Japan (April 9-13, 1988)

*Taipei Conference on Prostaglandin and Leukotriene Research*, Taipei, Taiwan, R.O.C. (April 22-24, 1988)

*FASEB Symposium on Oxy Radicals and Cytochrome P-450*, Las Vegas, Nevada (May 5, 1988)

*National Science Foundation Workshop of Physical Organic Chemistry (Reactive Intermediates)*, Lake Tahoe, California (May 21-23, 1988)

*Gordon Conference on Pyrroles*, Wolfeboro, New Hampshire (July 25-29, 1988)

*ASPET Symposium on Reactions of Hydroperoxides in Biological Systems*, Montreal, Quebec (October 11, 1988)

*Eleventh Enzyme Mechanisms Conference*, St. Petersburg, Florida (January 6-8, 1989)

*Winter Prostaglandin Meeting*, Keystone, Colorado (January 17-19, 1989)

*Symposium on Biological Oxidations*, American Chemical Society, Central Regional Meeting, Cleveland, Ohio (May 31-June 2, 1989)

*Risk Factors and Mechanisms in Carcinogenesis*, Joint Symposium of the Sonderforschungsbereiche 172 and 302, Wurzburg, West Germany (June 26-28, 1989)

*Eicosanoids and Bioactive Lipids in Cancer and Radiation Injury*, Detroit, Michigan (October 11-14, 1989)

*International Symposium on Biological Oxidation Systems*, Bangalore, India (October 22-26, 1989)

*DeChatelet Conference*, Bowman Gray School of Medicine, Winston-Salem, North Carolina (November 29, 1989)

*Fourth International Conference on Biological Reactive Intermediates*, Tuscon, Arizona (January 14-17, 1990)

*FASEB Symposium on Oxygen Radicals in Tissue Injury*, Washington, D.C. (April 2, 1990)

*VII International Conference on Prostaglandins*, Florence, Italy (May 28-June 1, 1990)

*VIII International Symposium on Microsomes and Drug Oxidations*, Stockholm, Sweden (June 25-29, 1990)

*Harden Conference on Free Radicals: Cell Growth, Disease and Repair Mechanisms*, Wye, England (September 2-7, 1990)

*Fourth Southeastern Regional DNA Symposium*, Oxford, Mississippi (October 26-27, 1990)

*Twenty First Symposium of the Princess Takamatsu Cancer Research Fund*, Tokyo, Japan (November 13-15, 1990)

*Symposium on the Role of Oxygen Free Radicals in Tissue Damage*, Kansas City, Missouri, (December 3-4, 1990)

*Symposium on Generation of Reactive Intermediates*, Canadian Federation of Biological Societies, Kingston, Ontario (June 11, 1991)

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*NIEHS Environmental Health Sciences Centers Directors Meeting*, Nashville, Tennessee, (June 17, 1991)

*International Symposium on Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Radiation Injury*, Berlin, Germany (September 18-21, 1991)

*Symposium on Peroxidases and Peroxyl Radicals in Toxicity*, Society of Toxicology Annual Meeting, Seattle, Washington (February 25, 1992) Also symposium cochairman.

*Twenty-Sixth European Symposium on Bioorganic Chemistry*, Gregynog, Wales (May 15-19, 1992), Plenary Lecture

*Eighth International Conference on Prostaglandins and Related Compounds*, Montreal, Canada (July 27-31, 1992) Also session chairman

*Eighteenth Symposium on Toxicology and Environmental Health*, Japanese Pharmacology Society (October 27, 1992) Plenary Lecturer

*Fourth North American Meeting of the International Society for the Study of Xenobiotics* Miami, Florida (November 5, 1992)

*DNA Adducts of Carcinogenic and Mutagenic Agents. Chemistry, Identification, and Biological Significance* Stockholm, Sweden (November 18-21, 1992)

*American Association of Cancer Research Special Conference "Chemicals, Mutations, and Cancer,"* Banff, Canada (December 7-12, 1992)

*American Association of Cancer Research Task Force on Chemoprevention Workshop*, Philadelphia, Pennsylvania (February 25, 1993)

*Fourth International Conference on Anticarcinogenesis and Radiation Protection*, Baltimore, Maryland (April 18-23, 1993)

*American Chemical Society Workshop on Chemical Mechanisms in Toxicology*, Washington, D.C. (August 2-4, 1993)

*Third International Conference on Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Radiation Injury*, Washington, D.C. (October 13-16, 1993)

*Workshop on Non-Steroidal Antiinflammatory Agents and Cancer* American Health Foundation, New York (October 28, 1993)

*American Chemical Society Workshop on Chemical Mechanisms in Toxicology*, Clearwater, Florida. (November 8-9, 1993)

*International Symposium on Molecular Biology of the Arachidonate Cascade*, Kyoto, Japan (December 6-7, 1993)

*American Association of Cancer Research Meeting on Risk Assessment in Environmental Carcinogenesis*, Whistler, British Columbia (January 17-22, 1994)

*American Cancer Society Workshop on NSAID's and Colon Cancer Prevention*, Atlanta, Georgia (March 21-22, 1994)

*Gordon Conference on Mutagenesis*, Plymouth, New Hampshire (June 27-July 1, 1994)

*International Union of Pharmacology*, Montreal (July 25-29, 1994)

*Thirteenth Symposium on Molecular Biology - Molecular Mechanisms of Toxicity*, Pennsylvania State University (August 3-5, 1994)

*Symposium on Radicals in Biochemistry and Chemistry*, Durham, North Carolina (September 16-17, 1994)

**Invited Lectures:**

1976

University of Michigan, Flint, Chemistry  
University of Michigan, Dearborn, Chemistry

1977

University of Michigan, Dearborn, Chemistry  
Oakland University, Chemistry  
University of Detroit, Chemistry  
Duke University, Pharmacology  
National Institute of Environmental Health Sciences

1978

Cleveland State University, Chemistry  
University of Wisconsin, Madison, College of Pharmacy  
University of Toledo, Chemistry  
Ohio University, Chemistry  
Veteran's Administration Geriatric Research Center, St. Louis

1979

Wayne State University, Chemistry  
Lawrence Institute of Technology, Chemistry  
Ohio Wesleyan University, Chemistry  
Michigan State University, Pharmacology and Toxicology  
University of Michigan, Dearborn, Natural Sciences

1980

University of Texas Health Sciences Center, Dallas, Biochemistry  
University of Detroit, Chemistry  
Wayne State University, Biochemistry  
St. John Fisher College, Chemistry  
Niagara University, Chemistry  
University of Rochester, Chemistry  
National Institute of Environmental Health Sciences

1981

Ford Motor Company, Dearborn, MI  
Mercy College, Chemistry  
University of Texas Health Sciences Center, Dallas, Biochemistry  
North Texas State University, Chemistry  
Wayne State University, Chemistry  
Michigan Cancer Foundation  
McArdle Laboratory for Cancer Research, University of Wisconsin, Madison  
New York Medical College, Pharmacology  
Western Michigan University, Chemistry  
Hope College, Chemistry  
Detroit Physiological Society

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1982

Warner-Lambert/Parke-Davis  
The Upjohn Company  
Hoffmann-LaRoche  
Wayne State University, Biology  
Wayne State University, Pharmacology  
University of Chicago, Chemistry  
Bayer Pharmaceuticals, Wuppertal, West Germany  
Federal Cancer Research Center, Heidelberg, West Germany  
Wayne State University Medical School, Biochemistry  
Oakland University  
Pfizer Central Research  
Massachusetts Institute of Technology, Department of Nutrition and Food Science

1983

University of California, San Francisco, Pharmaceutical Chemistry  
University of California, Berkeley, Biochemistry  
University of Rochester, Pharmacology  
University of Rochester Cancer Center  
University of Michigan, School of Public Health  
Central Michigan University  
University of Toledo, Chemistry  
Frederick Cancer Research Institute

1984

National Institute of Environmental Health Sciences  
Oakland University, Chemistry  
Wayne State University, Chemistry  
Northwestern University School of Medicine, Pharmacology  
University of Virginia, Chemistry  
University of Guelph, Chemistry  
Ecole Normale Supérieure, Chemistry, Paris, France  
University of Strasbourg, Molecular Biology  
University of Michigan School of Public Health  
American Cancer Society Workshop, Traverse City Workshop  
Vanderbilt University School of Medicine, Biochemistry  
University of Detroit, Chemistry  
Kochi University School of Medicine, Biochemistry, Kochi, Japan  
Keio University School of Medicine, Biochemistry, Tokyo, Japan  
University of Phillipines School of Medicine, Manila, The Phillipines.  
University of Phillipines, Chemistry, Quezon City, The Phillipines.

1985

University of Rochester, Chemistry  
Harvard Medical School, Biological Chemistry  
Wayne State University, School of Medicine, Physiology

1986

Case Western University, Chemistry  
Pennsylvania State University, Biochemistry  
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University of Texas System Cancer Center

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University of Texas, Austin, Chemistry  
Johns Hopkins University, Environmental Health Sciences  
Washington State University, Chemistry  
University of Toronto, Pathology  
University of Minnesota, Chemistry  
Wayne State University, Food Science and Nutrition  
Medical College of Wisconsin, Biochemistry  
University of Alberta Cancer Center  
Vanderbilt University, Biochemistry  
Vanderbilt University, Center for Molecular Toxicology

1987

Massachusetts Institute of Technology, Applied Biological Sciences  
Health Effects Institute  
Warner-Lambert/Parke-Davis, Biochemistry Division  
Michigan State University, Biochemistry  
University of California-Berkeley, Biochemistry  
Eppley Institute for Cancer Research  
University of Colorado-Boulder, School of Pharmacy  
University of California San Francisco, School of Pharmacy  
University of Michigan, Biological Chemistry  
Duke University, Chemistry  
Wayne State University, Pathology  
Indiana University, Chemistry  
Northeast Regional American Chemical Society Medicinal Chemistry Group  
Wayne State University, Biochemistry

1988

University of Utah, Chemistry  
Wayne State University, Chemistry  
Oakland University, Chemistry  
Searle Research and Development  
Tokyo University, Pharmaceutical Sciences  
National Cancer Center, Tokyo, Biology Division  
National Yang Ming Medical College, Taipei, Institute for Biochemistry  
University of Guelph, Chemistry  
University of Guelph, Nutrition  
Michigan Cancer Foundation  
Vanderbilt University, Chemistry  
Vanderbilt University, Biochemistry

1989

Wayne State University, Pharmacology  
University of Toledo, Medicinal Chemistry  
Vanderbilt University, Center in Molecular Toxicology  
Vanderbilt University, Program in Molecular Biophysics  
Bowman Gray School of Medicine, Cancer Center

1990

Vanderbilt University, Molecular Biology  
University of Cincinnati, Institute of Environmental Health  
M.D. Anderson Cancer Center and Tumor Institute, Cell Biology

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University of Texas, College of Pharmacy  
University of Pennsylvania, Pharmacology  
Vanderbilt University, Pharmacology  
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Wellcome Research Laboratories, Division of Pharmacology  
Tokushima University, Biochemistry  
Ono Pharmaceutical Research Laboratories  
Tokyo University, Department of Plant Chemistry and Pharmacognosy  
Tokyo Metropolitan Institute of Aging  
Upjohn Company, Tsukuba Research Laboratories  
Emory University, Biochemistry

1991

Vanderbilt University, Pharmacology  
Vanderbilt University, Center in Molecular Toxicology  
University of Texas Southwestern Medical School at Dallas, Pharmacology  
Vanderbilt University, Biochemistry  
American Health Foundation  
Cornell University Medical Center, Pharmacology  
Schering Pharma, Berlin  
American Chemical Society, Lexington Section, Lexington, Kentucky  
University of Louisville Medical School, Biochemistry  
Vanderbilt University, Center in Molecular Toxicology Open House  
Rhodes College, Chemistry  
Belmont University, Chemistry  
Vanderbilt University, Center in Molecular Toxicology

1992

University of California San Francisco, Pharmaceutical Chemistry  
Vanderbilt University, Medicine - Oncology Division  
Vanderbilt University, Medicine - Nephrology Division  
National Institute of Environmental Health Sciences  
Vanderbilt University, Center in Molecular Toxicology  
Vanderbilt University, Center in Molecular Toxicology Open House  
Tokyo College of Pharmacy, Tokyo  
National Institute of Hygienic Sciences, Tokyo  
Karolinska Institutet, Stockholm, Medical Chemistry

1993

University of Texas Health Science Center, San Antonio, Biochemistry  
Mallinckrodt Medical Products  
Vanderbilt University School of Medicine, Pathology  
University of Nebraska, Chemistry  
Vanderbilt University, Chemistry  
Rutgers University, Chemical Biology and Pharmacognosy  
Vanderbilt University School of Medicine, Center in Molecular Toxicology  
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Western Maryland College, Chemistry  
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Banyu Pharmaceutical, Tsukuba, Japan  
Tokyo University, Center for Advanced Research

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Vanderbilt University School of Medicine, Clinical Pharmacology

1994

University of Arizona, Southwest Center for Environmental Health Sciences  
Vanderbilt University School of Medicine, Center in Molecular Toxicology  
University of Arkansas Medical School, Pharmacology and Toxicology  
Institut Gustave-Roussy, Pharmacologie Moleculaire  
Universite Rene Descartes, Laboratoire de Chimie et Biochimie  
Schering-Plough

## PUBLICATIONS

### Refereed Journals:

1. N. A. Porter, M. E. Landis, and L. J. Marnett, "The Photolysis of Unsymmetric Azo Compounds," *J. Amer. Chem. Soc.*, **93**, 795-796 (1971).
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9. L. J. Marnett, G. A. Reed, and J. T. Johnson, "Prostaglandin Synthetase-Dependent Benzo[a]pyrene Oxidation: Products of the Oxidation and Inhibition of Their Formation by Antioxidants," *Biochem. Biophys. Res. Comm.*, **79**, 569-576 (1977).
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